

REMARKS/ARGUMENTS

Applicants have cancelled claims 7-9 without prejudice. Applicants have amended claims 2, 4-6 for the purpose of expediting the issuance of claims. Claim 2 has been amended to correct grammatical errors. In addition claim 2 has been amended to clarify that the subject being diagnosed by comparison to samples of matched reproductive state is female. Support for this amendment may be found throughout the specification and particularly at page 23, lines 25-26. Claims 4 and 5 have been similarly amended to clarify that the experimental sample is from a female.

Claim 4 has been amended to clarify that the reference samples that are used to generate the average expression profile are matched in at least one indicator of reproductive status and to clarify that the experimental sample is diagnosed with a physiological disorder by comparing the gene expression profile to an average gene expression profile. Support for the amendments may be found throughout the specification, for example on page 15, lines 27-30. The specification also teaches that an experimental sample is compared to reference samples of known disease states and the experimental sample is diagnosed with the disease of the matching reference sample(s) (page 18, lines 3-9).

Claim 5 has been amended to clarify that it is a method to identify the reproductive status as indicated in the preamble. In addition the claim has been amended to recite a final process step that clearly relates back to the preamble. Specifically the phrase "using said expression profile" has been replaced with the phrase "by identifying an expression profile of known reproductive status that is similar to the expression profile from the experimental sample." The methods of the invention generally involve comparing gene expression profiles from experimental samples to gene expression profiles from samples of known status to identify the status of the experimental sample by identifying a similar sample of known status. In claim 5 it is the reproductive status that is being determined.

Claim 6 has been amended to clarify that gene expression profiles are obtained from different reproductive states and compared to identify genes that are differentially expressed between the two states. The final step has been amended to clarify that the markers identified are of different reproductive states in women.

It is respectfully submitted that no new matter has been introduced by the present amendments and entry of the same is respectfully requested. Applicants respectfully request reconsideration of the pending rejection and reexamination of the present claims in light of the amendments and the remarks detailed below.

By these amendments, the Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which Applicants are entitled.

35 U.S.C. § 112 Rejection

In Paragraph 3A) of the office action the examiner has rejected claims 2 and 4-9 under 35 U.S.C. 112, second paragraph as being indefinite because "it is uncertain as to what encompasses 'reproductive state'" Applicants respectfully disagree. One of skill in the art would understand that reproductive state entails parameters that are related to the normal variations in reproductive events. This includes whether or not a woman is or has ever been pregnant and if so, how many pregnancies and the outcome of those pregnancies, whether a woman has lactated and if so for how long, whether a woman is pre-menopausal, peri-menopausal, menopausal or post-menopausal and what phase of the menstrual cycle the individual was in when the sample was isolated. In an effort to clarify the meaning of "reproductive state" Applicant's have amended the paragraph beginning at page 5, line 21 of the specification. Applicants believe that the amendments do not introduce new matter and simply make explicit what would have been known by one of skill in the art to be meant by "reproductive state". Additional examples have been included for clarity.

In Paragraph 3B) the Examiner indicates that "reproductive state" and "reproductive status" are not defined in the specification. As indicated above Applicants believe that it would be clear to one of skill in the art what parameters would be included in determining reproductive state, but Applicants have amended the specification as indicated above to clarify which parameters would be included.

Claims 7-9 have been canceled making the rejection of these claims in paragraph 3C) moot. Claim 6 is not dependent on claim 5.

Claims 5 and 6 have been amended to recite a final process step which clearly relates back to the preamble as suggested in paragraph 3D).

Anticipation Rejection Under 35 U.S.C. § 102(e)

The Examiner has rejected claims 2 and 4-6 under 35 U.S.C. 102(e) as being anticipated by Friend *et. al.*, (US 6,218,122). Applicants respectfully traverse this rejection.

Applicants have amended the specification to remove ambiguity in the terms "reproductive state" and "reproductive status". Matching samples simply by sex or age is not identical to matching samples according to at least one parameter of reproductive status. Matching the reproductive status of samples presupposes that the samples are from females and requires at least one additional matching parameter that reflects reproductive state, for example, menopausal or post-partum women. Applicants respectfully submit that Friend *et. al.* does not disclose comparing gene expression of samples with matching reproductive state. Therefore, the rejection under 102(e) should be withdrawn.

CONCLUSION

For these reasons, Applicants believe all pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5768. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

Respectfully submitted,



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